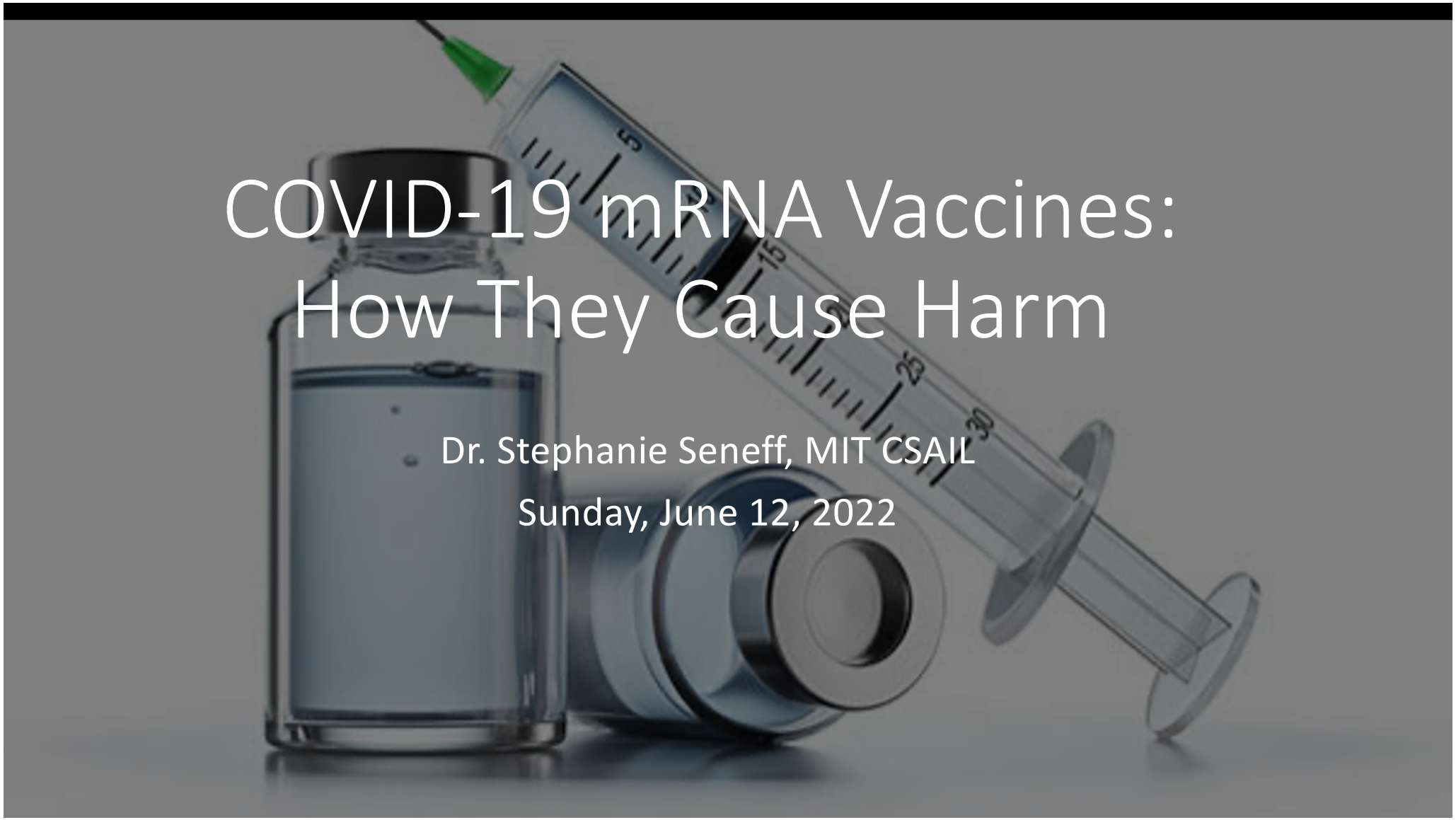


COVID-19 mRNA Vaccines: How They Cause Harm

Dr. Stephanie Seneff, MIT CSAIL

Sunday, June 12, 2022

Outline

- Overview
- Neurodegenerative Disease
- Syncytia and Senescence
- Myocarditis and Heart Issues
- Summary

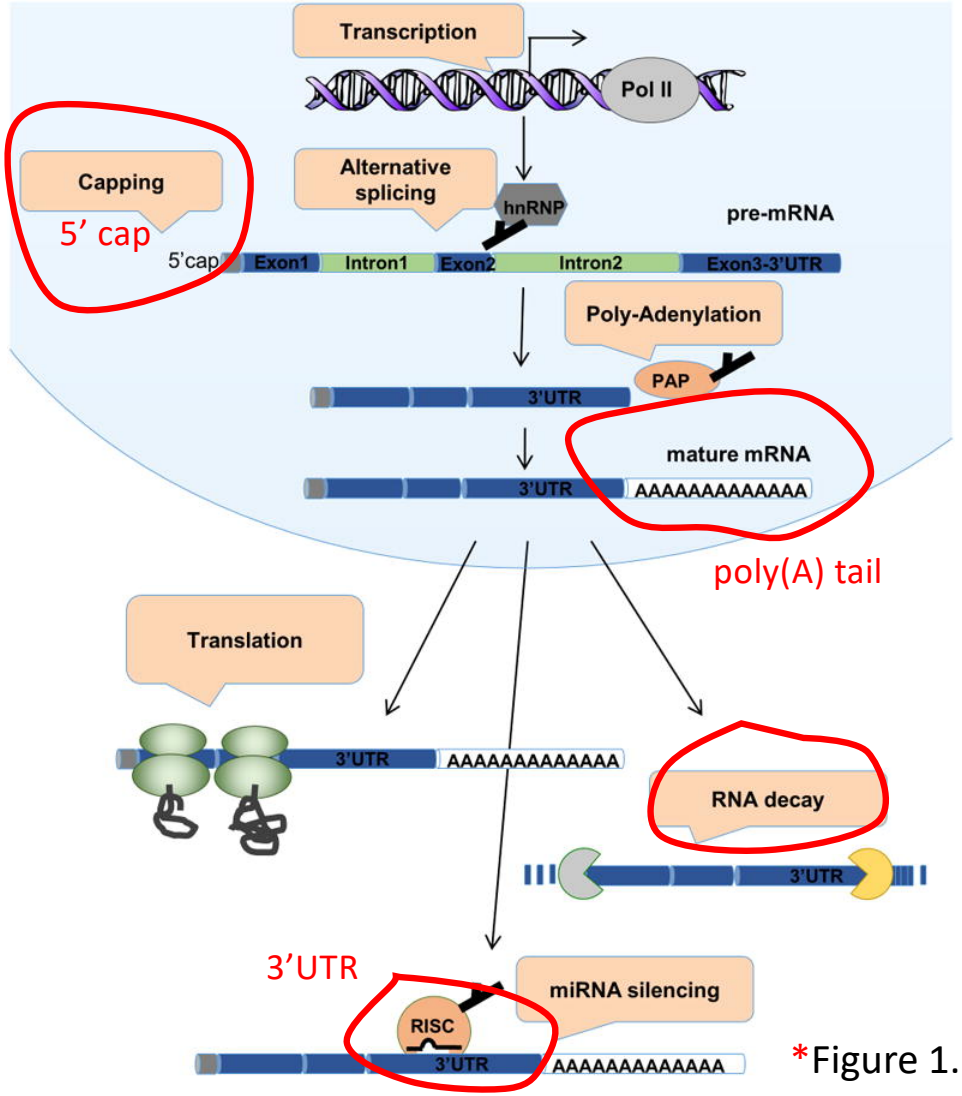
“Worse than the Disease? Reviewing Some Possible Unintended Consequences of the mRNA Vaccines Against COVID-19” *

The mRNA vaccines are a poorly evaluated novel technology with many unknowns

Some potential adverse consequences:

- Pathogenic priming, multisystem inflammatory disease and autoimmunity
- Allergic reactions and anaphylaxis
- Antibody dependent enhancement
- Activation of latent viral infections
- Neurodegeneration and prion diseases
- Emergence of novel variants of SARS-CoV-2
- Potential for integration of the spike protein gene into human DNA

*S Seneff and G Nigh. IJVTPR May 2021; 2(1): 38-79.

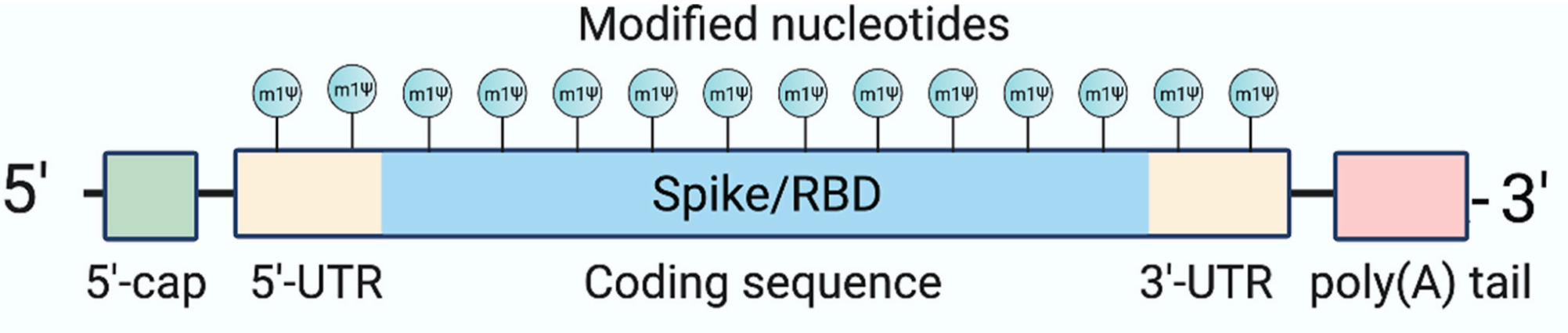


The RNA Life Cycle*

The mRNA vaccines are cleverly designed to contain mRNA that is perfectly set up to churn out spike proteins with no way to turn off the spigot

- 5’ cap and long poly(A) tail added to make it look like a human protein
- Modified nucleotides to resist breakdown (1-methyl-pseudouridine)
- Select hearty 3’UTR to resist silencing
- Codon optimization to promote rapid protein synthesis

*Figure 1. Florian J. Bock et al. Mol Cell. 2015 June 18; 58(6): 959–969.



- mRNA vaccines contain the genetic code to make spike protein
- The RNA is carefully engineered to resist breakdown
  - All of the uridines are replaced with 1-methyl-pseudouridine (m1Ψ)
- The mRNA is incorporated into a lipid particle along with polyethylene glycol (PEG)
- A synthetic cationic (positively charged) lipid is added as an adjuvant – very toxic to the cells
- The "humanized" mRNA is a stealth entry system for massive production of spike protein

*S Seneff and G Nigh. IJVTPR May 2021; 2(1): 38-79.

Food and Chemical Toxicology 164 (2022) 113008

Contents lists available at ScienceDirect

Food and Chemical Toxicology

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"In this paper, we present evidence that vaccination induces a profound impairment in type I interferon signaling, which has diverse adverse consequences to human health."

"These disturbances potentially have a causal link to neurodegenerative disease, myocarditis, immune thrombocytopenia, Bell's palsy, liver disease, impaired adaptive immunity, impaired DNA damage response and tumorigenesis."

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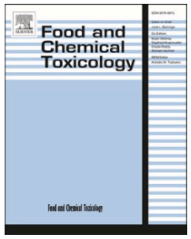

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The Big Picture

- A natural infection starts in the nose and lungs and never makes it into general circulation if the immune system is healthy
- Injection of spike mRNA nanoparticles into deltoid muscle bypasses mucosal and vascular barriers
- Immune cells take up mRNA nanoparticles and carry them into the lymph system, ultimately into the spleen
- Immune cells in the spleen release large quantities of spike protein displayed on the surface of exosomes
  - These exosomes disperse throughout the body, but, especially, travel to the brain to deliver the toxic prion-like spike protein to neurons
  - Inflammatory response in the brain induces neurological damage
- The spike protein induces syncytia formation and senescence in exposed cells
- Spike protein damages the heart, inducing cardiovascular disease

Neurodegenerative Disease

Trends Neurosci. 2020 Dec; 43(12): 931–933.
Published online 2020 Oct 21. doi: 10.1016/j.tins.2020.10.009

Is COVID-19 a Perfect Storm for Parkinson's Disease?

Patrik Brundin,[1,*] Avindra Nath,[2] and J. David Beckham[3]

- Loss of smell is a common early symptom of Parkinson's and of COVID-19
- The virus can gain access to the brain along nerve fibers
  - Olfactory nerve
  - Vagus nerve
- Neuroinvasion of SARS-COV-2 could upregulate α-synuclein
  - High levels of α-synuclein leads to misfolding and toxicity
- Dopaminogenic neurons in substantia nigra express high levels of the ACE2 receptor

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- Dopaminogenic neurons in substantia nigra express high levels of the ACE2 receptor

Three independent case reports have described the development of Parkinson's disease following COVID-19.*

* Ernesto Estrada *Viruses* 2021; *13:* 897.

"Nucleoside-modified mRNA vaccines induce potent T follicular helper and germinal center B cell responses"*

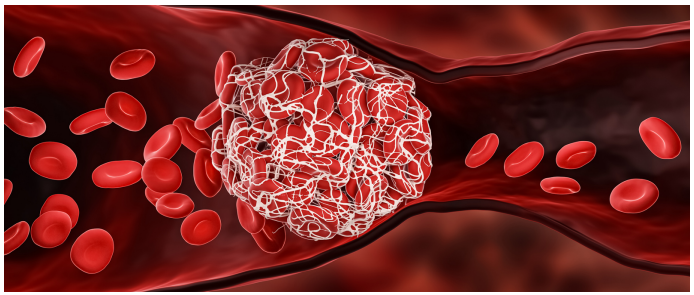
- "Nucleoside-modified" means that all the uridines in the mRNA were replaced with 1-methyl-pseudouridine
  - This replacement resulted in robust synthesis of protein from the mRNA code (protected RNA from degradation)
- Result was a very strong antibody response due to formation and maintenance of *germinal centers in the spleen*
- Another study showed that repeated exposure to antigen (foreign protein) through immunization resulted in increased susceptibility to prion protein exposure**
  - Attributed to *expansion of splenic germinal centers*

*Norbert Pardi et al. J. Exp. Med. 2018 Vol. 215 No. 6 1571–1588

**Juliane Bremer et al., PLoS ONE 2009; 4(9): e7160.

The mRNA in the vaccines is long-lasting and induces strong IgG response*

- Lymph nodes of vaccine recipients show abundant germinal centers
- Vaccination induces *stronger IgG response* than the disease
- The mRNA from the vaccines and spike proteins remain in germinal centers in lymph nodes for up to 60 days



A strong IgG response can lead to platelet activation and blood clots!!

*Katharina Röltgen et al. Cell 2022; 185(6): 1025-1040.

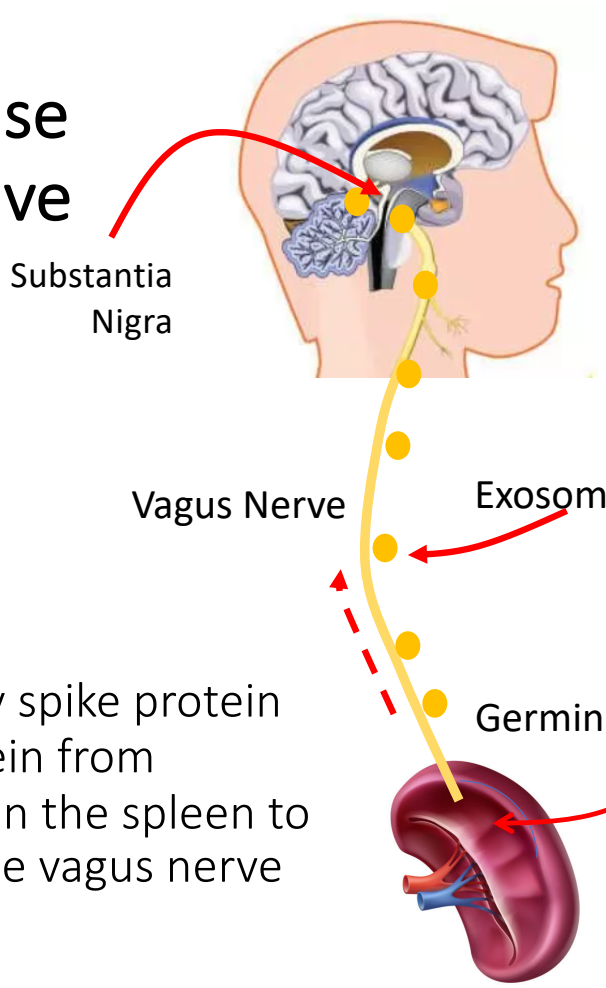
Exosomes and Parkinson's Disease*

- Parkinson's disease often begins in the gut as an immune reaction to prion-like proteins produced by pathogens
- The spike protein is a prion-like protein
  - It contains 7 glycine zippers (GxxxG) – a characteristic signature of prions

  (The human prion protein contains 14, and amyloid beta (linked to Alzheimer's disease) contains only 4)
- Stressed immune cells in the digestive tract and spleen upregulate α-synuclein and release it packaged up in exosomes, along with foreign misfolded proteins
- The exosomes travel along the vagus nerve to the brain stem nuclei
- Damage to the substantia nigra causes Parkinson's disease
- The whole process can take years or decades before symptoms appear

*S Seneff and G Nigh. IJVTPR 2021; 2(1): 38-79.

How mRNA Vaccines can Cause Neurodegenerative Disease



3. Spike protein and alpha synuclein taken up by neurons in the substantia nigra are neurotoxic – increased future risk to Parkinson's disease

2. Exosomes carry spike protein and alpha-synuclein from germinal centers in the spleen to the brain along the vagus nerve

1. Immune cells in the spleen stressed by excess spike synthesis release exosomes containing spike protein

Symptoms in VAERS in 2021 for conditions related to vagus nerve damage*

Symptom	COVID-19 Vaccines	All Vaccines	Percent COVID-19
Anosmia	3,657	3,677	99.5
Tinnitus	13,275	13,522	98.2
Deafness	2,895	3,033	95.5
Bell's Palsy/facial palsy	5,881	6,129	96.0
Vertigo	7,638	7,819	97.7
Migraine headache	8,872	9,059	97.9
Dysphonia	1,692	1,751	96.6
Dysphagia	4,711	4,835	97.4
Nausea	69,121	7,1275	97.0
Vomiting	27,885	28,955	96.3
Dyspnea	39,551	40,387	97.9
Syncope	14,701	15,268	96.3
Bradycardia	673	699	96.3
TOTAL	**200,552**	**206,409**	**97.2**

loss of smell

*S Seneff et al. Food and Chemical Toxicology 2022; 164: 113008.

SARS-CoV-2 Spike Activates Human Microglia in the Brain via Exosomes Loaded with miRNAs*

- "SARS-CoV-2 spike transfected cells release a significant amount of exosomes loaded with microRNAs such as miR-148a and miR-590”
- "MicroRNAs get internalized by human microglia in the brain”
  - Induce a strong inflammatory response
- "These results uncover a bystander pathway of SARS-CoV-2 mediated CNS [central nervous system] damage through hyperactivation of human microglia"

*Ritu Mishra and Akhil C. Banerjea. Frontiers in Immunology 2021; 12:656700

Exosome Transfer from Cell to Cell*

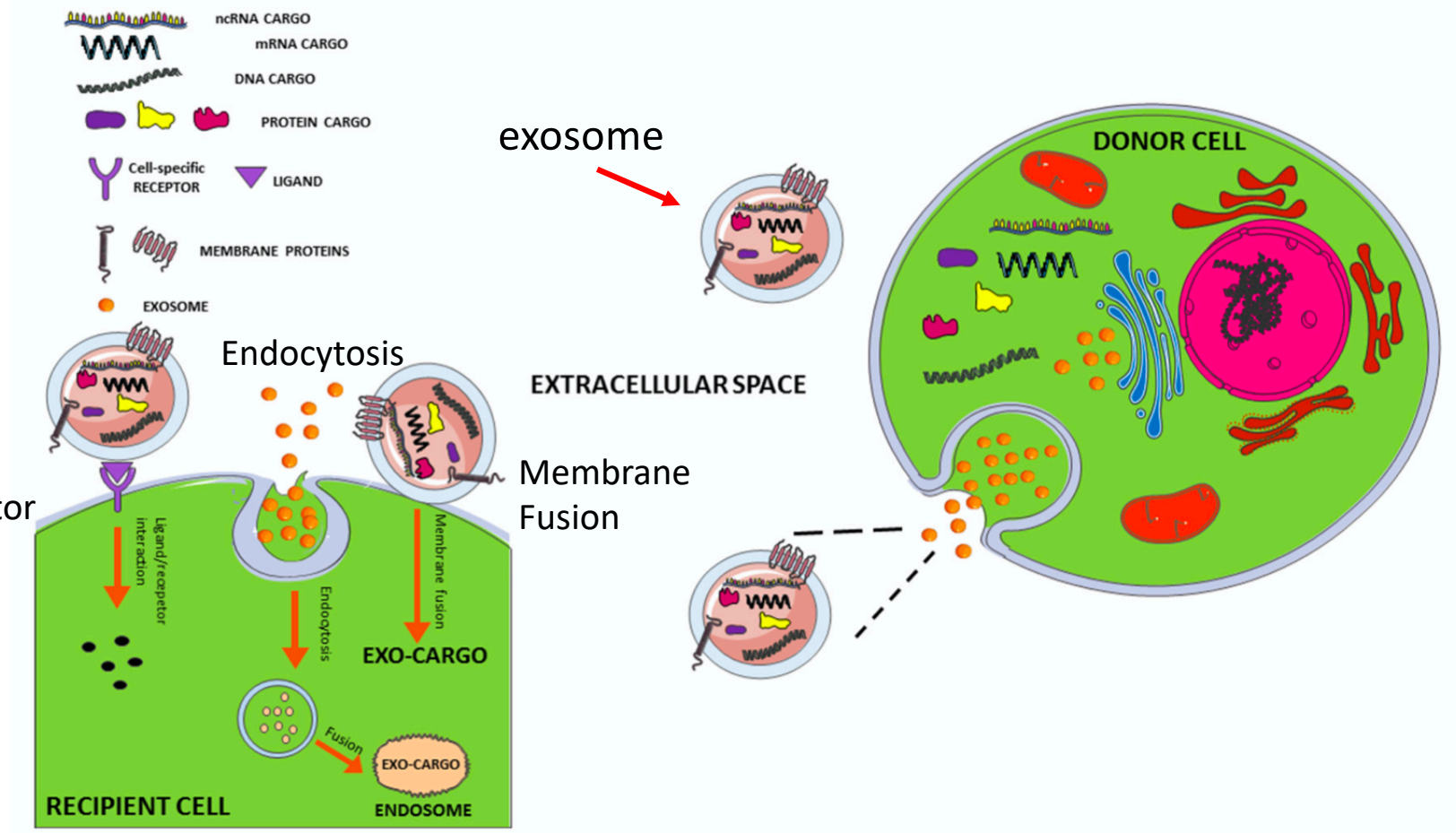


*Figure 1. Marianna D'Anca et al. Front. Aging Neurosci. 28 August 2019; 11: 232.

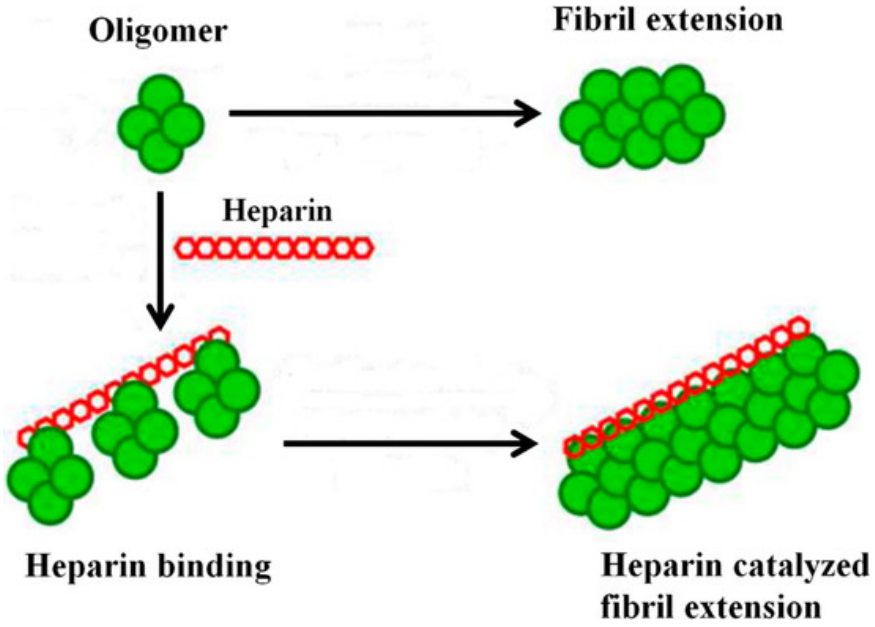
Problems with the vaccine spike protein*

- "Is it possible the spike protein itself causes the tissue damage associated with Covid-19?”
- A “furin cleavage site” in the spike protein allows S1 subunit to be snipped off and released into circulation
- The S1 subunit localizes to the endothelia of microvessels in the mouse brain and is a potent neurotoxin."
- "So the spike S1 subunit of SARS-CoV-2 alone is capable of being endocytosed by ACE2 positive endothelia in both human and mouse brain, with a concomitant paucicellular microencephalitis that may be the basis for the neurologic complications of COVID-19."

*https://beta.regulations.gov/document/FDA-2020-N-1898-0246
Comment from J. Patrick Whelan MD PhD
Food and Drug Administration on Dec 8, 2020

"SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration"*

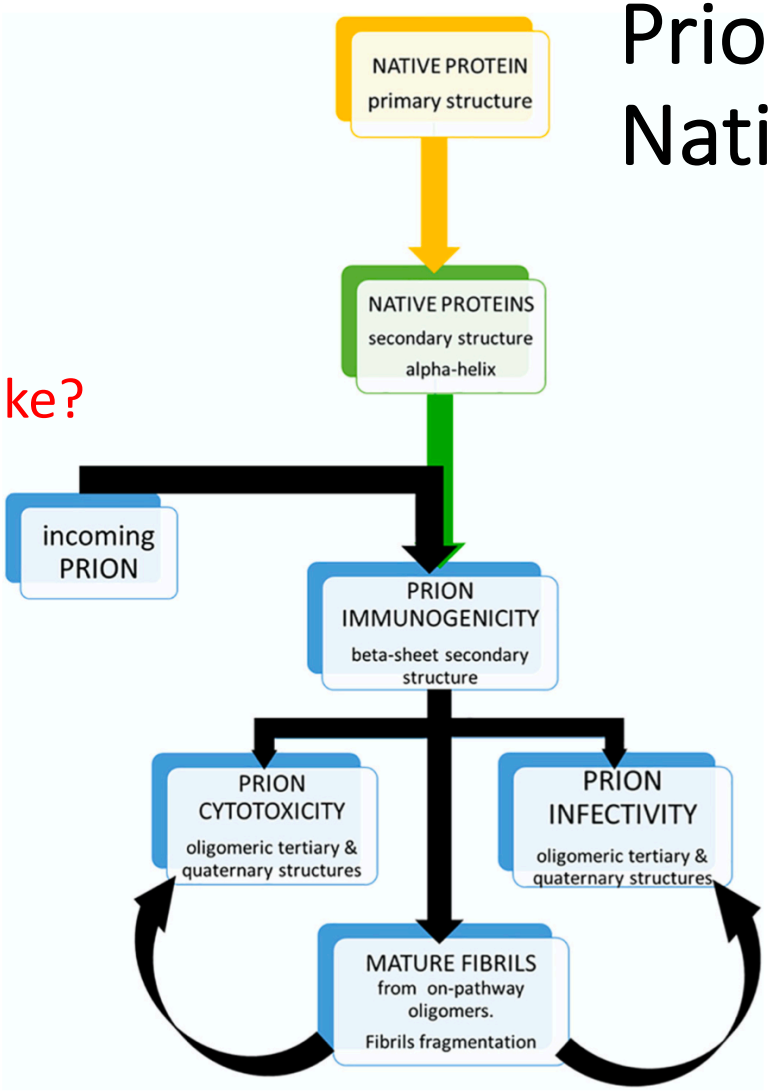
- The receptor binding domain (RBD) of the spike protein binds to heparin and to heparin-binding proteins
- Heparin binding accelerates aggregation of amyloid proteins
  - Amyloid-β, α-synuclein, tau, prion and TDP-43
- This could lead to neurodegeneration in the brain



*D Idrees and V Kumar. Biochemical and Biophysical Research Communications 2021; 554: 94e98.

Prion Corruption of Natively Folded Proteins*

Spike?



- Foreign prion proteins (e.g., spike) act like crystals to induce misfolding of susceptible human proteins (e.g., α-synuclein, amyloid-β, etc.)
- Proteins change from α-helix to β-sheet configuration
- This leads to formation of oligomers and fibrils → neurodegenerative disease (Parkinson's, Alzheimer's, ALS, CJD, ..)

*Dana Butnaru and Joab Chapman. Autoimmun Rev 2019; 18(3): 231-240.

"COVID-19 Vaccine Associated Parkinson's Disease, A Prion Disease Signal in the UK Yellow Card Adverse Event Database."*

"All the COVID-19 vaccines on the market contain spike protein or its nucleic acid sequence creating a possible catastrophic epidemic of prion disease in the future."

"This analysis should serve as an urgent warning to those mindlessly following advice of politicians and public health officials regarding COVID immunization."

*J Bart Classen. J Med - Clin Res & Rev. 2021; 5(7): 1-6.

VAERS Adverse Events, 2021*

Condition	COVID vaccines (2021)	All vaccines (2021)	Percent COVID
Memory Impairment	1681	1720	97.7
Amnesia	1360	1419	95.8
Mobility Decreased	8974	9742	92.1
Alzheimer's	37	39	94.9
Parkinson's Disease	91	97	93.8
Dysphagia (Difficulty Swallowing)	4711	4835	97.4
Anosmia (Loss of Smell)	3657	3677	99.5

*US Vaccine Adverse Event Reporting System: http://wonder.cdc.gov/vaers.html

PREMIUM **HEALTH NEWS**

Studies Link Incurable Prion Disease With COVID-19 Vaccines*

By Marina Zhang | June 4, 2022 Updated: June 7, 2022 Print

- Prion-like region exists in original Wuhan variant of COVID-19 but it has been lost in the omicron variant
- A preprint paper (Prof. Luc Montagnier is an author) reviewed 26 cases of Creutzfeldt Jakob Disease developing within a month of the second COVID vaccine
  - All of the patients deteriorated very quickly, and they are all now dead
- A peer-reviewed study in Turkey described a case of CJD where symptoms appeared just one day after a Sinovac vaccine

*https://www.theepochtimes.com/mkt_app/studies-link-incurable-prion-disease-with-covid-19-vaccine_4511204.html

Anecdotal Evidence: Marc Doyer (in France) testified that his wife developed Creutzfeldt Jakob disease about two weeks after her second dose of the Pfizer mRNA vaccine *

> "We must no longer speak of chance, because when you develop a disease where it is said that there is one case in a million, and less than sixty cases per year in France, and that you develop the first symptoms 15 days after the second injection of a vaccine that we do not know well, we can no longer afford to speak of chance."

* https://news.in-24.com/lifestyle/tv/148758.html

Syncytia and Senescence

"Senescence-associated inflammatory responses: aging and cancer perspectives"*

- Senescence is a cellular response to injury resulting in permanent arrest of the cell cycle (irreversible)
- Senescence-Associated Secretory Phenotype (SASP)
  - Senescent cells are metabolically active and express a vast number of secreted proteins that exert a paracrine effect on other cells
- Secreted inflammatory cytokines and chemokines link senescence to inflammation

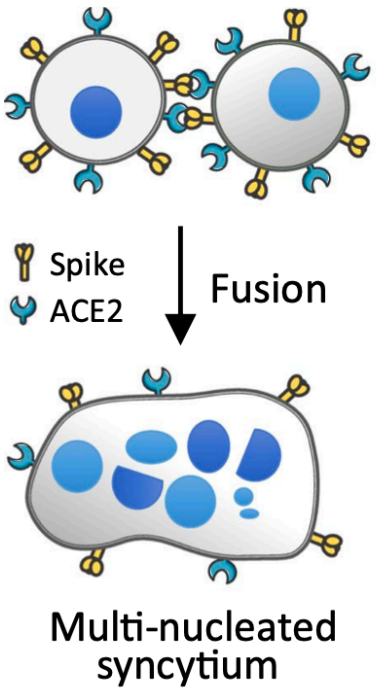
*Audrey Lasry and Yinon Ben-Neriah. Trends in Immunology 2015; 36(4): 217-228.

“Virus-induced senescence is a driver and therapeutic target in COVID-19”*

- SARS-CoV-2 invokes a cellular senescence response in infected cells
  - Accompanied by SASP
  - Includes pro-inflammatory cytokines, extracellular-matrix-active factors and pro-coagulatory mediators
- Secondary senescence of endothelial cells caused by SASP secretions into the vasculature
- Supernatant from infected cells induced platelet activation and the clotting cascade

*Soyoung Lee et al. Nature 2021; l599: 283-289.

“Micronucleus production, activation of DNA damage response and cGAS-STING signaling in syncytia induced by SARS-CoV-2 infection”*



- Experiments conducted on Hela-ACE2 cells grown in culture
- Exposure to SARS-CoV-2 spike glycoprotein, mediated by ACE2, induces cell-cell fusion
  → multi-nucleated syncytium formation
- Syncytia succumb to DNA damage and genomic instability, resulting in appearance of micronuclei
- This results in activation of the cGAS-STING signaling pathway and SASP, a prototypical senescent phenotype

*He Ren et al. Biol Direct 2021; 16: 20.

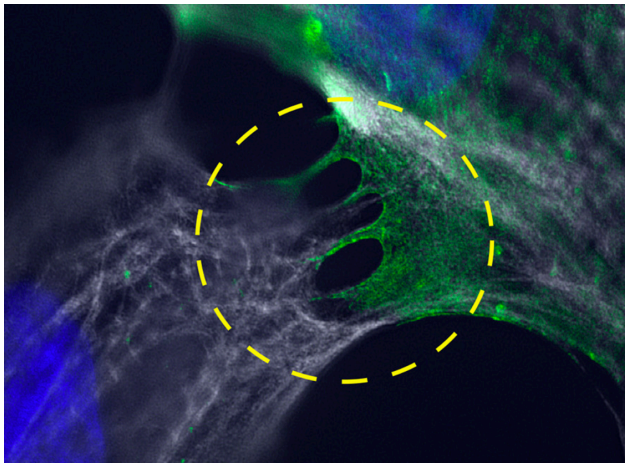
"Role of senescence in the chronic health consequences of COVID-19”*

"Innate immune system dysfunction that leads to decreased senescent cell removal and/or increased senescent cell formation could contribute to accumulation of senescent cells with both aging and viral infections."

*Erin O Wissler Gerdes et al. Translational Research 2022; 241: 96-108.

SARS-CoV-2 infects cardiomyocytes and induces syncytia formation*

- Human cardiomyocytes contain abundant ACE2
- SARS-CoV-2 replicates efficiently in cardiomyocytes
- Viral transcripts accounted for 88% of total mRNA
- Virus-like particles with knob-like spikes covered the cell surface.
- *Viral spike protein induces filopodia formation and fuses cardiomyocytes, generating syncytia*
- Furin cleavage site essential for syncytia formation
- Abundant progeny virions found in exocytic vesicles



Filopodia linking two cardiomyocytes

*Chanakha Navaratnarajah et al. Journal of Virology 2021; 95(24): e01368-21

Aging, cellular senescence, and COVID-19*

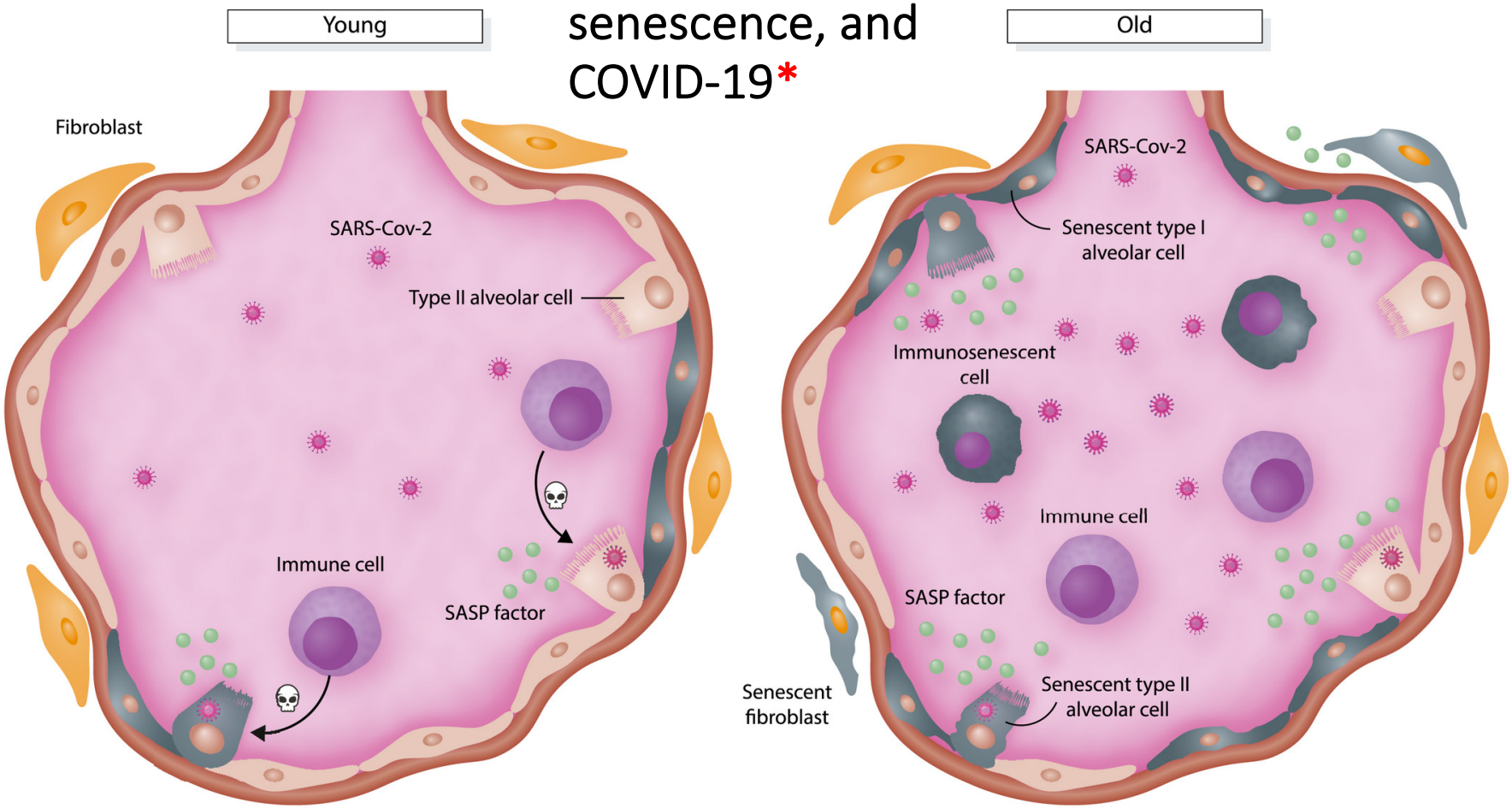


*Figure 4. Jaskaren Kohli et al. EMBO Reports (2021)22:e52243

EMBO

“SARS-CoV-2 Infection Causes Dopaminergic Neuron Senescence”*

- SARS-CoV-2 infection triggers a dopaminergic neuron inflammatory and cellular senescence response
  - Confirmed through analysis of human ventral midbrain tissue from COVID-19 patients
- Dopaminergic neurons express ACE2 and promote viral proliferation
- A high-throughput screen identified several FDA approved drugs, including riluzole, metformin, and imatinib, that can rescue the cellular senescence phenotype

*Shuibing Chen et al. Research Square preprint. May 21, 2021. doi: 10.21203/rs.3.rs-513461/v1

Myocarditis and Heart Issues

Hypothesis

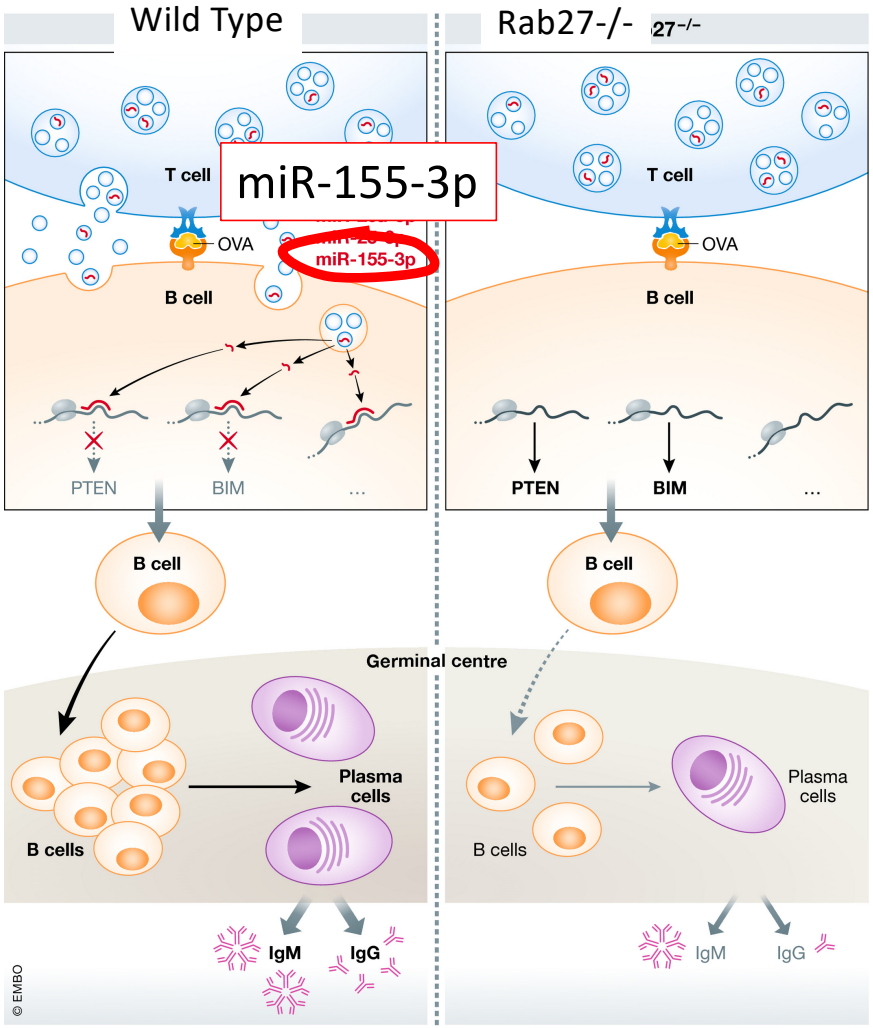
- Immune cells in the spleen, transfected with the mRNA vaccine, make abundant amounts of spike protein that they release within exosomes, packaged up along with microRNAs that impact recipient cells
- Exosomes travel along the vagus nerve to the heart, delivering spike protein and signaling miRNAs
- Exosomes taken up by immune cells in the heart induce an inflammatory response
- Fibroblasts in the heart become senescent, leading to cardiac rupture and other cardiac symptoms

“Exosomes take (germinal) center stage”*

- Horizontal transfer of *microRNAs* via *exosomes* from T to B cells is necessary for germinal center formation and efficient antibody production
- *miR-155-3p* silences PTEN and BiM, supporting B cell maturation and proliferation
- *However, miR-155 is also associated with many autoimmune diseases***

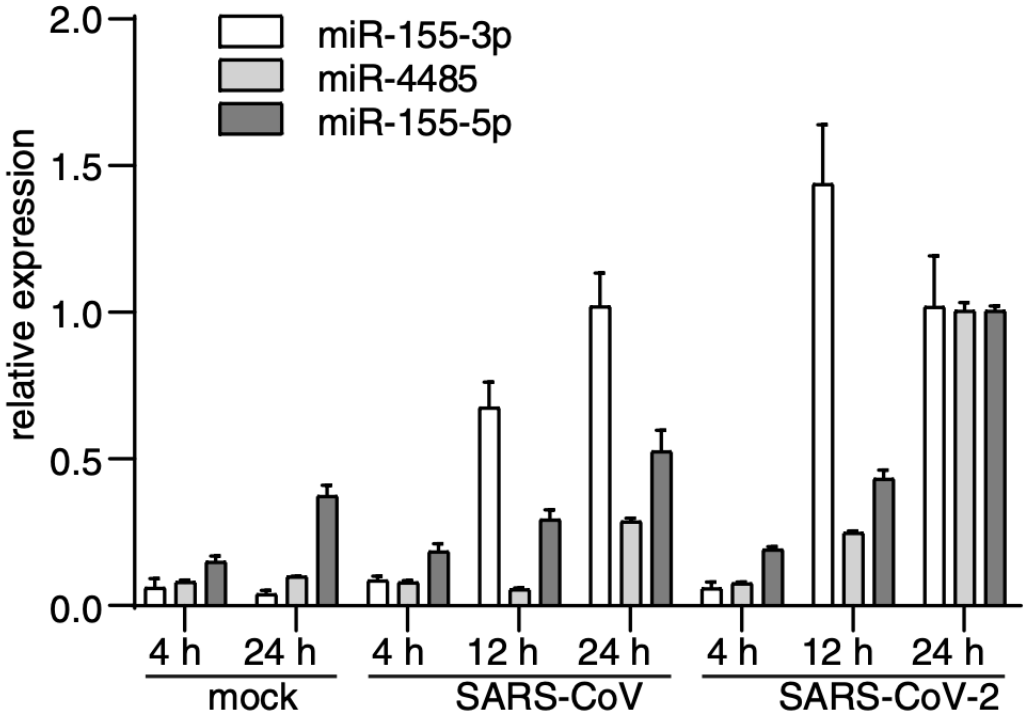
*Figure 1. Jennifer Pérez-Boza and Dirk M Pegtel. EMBO Rep 2020; 21: e50190

**Salar Pashangzadeh et al. Frontiers in Immunology 2021; 12: 669382



Rab27 is essential for exosome secretion

A role for miRNA-155 in SARS-CoV-2*



- Comparison between SARS-CoV and SARS-CoV-2
- “Small RNA profiling indicated an increased expression of miR-155 in the infected cell”
- "We found strong induction of miR-155 with both viruses, suggesting a role for this miRNA in the progression of infection.”

*Emanuel Wyler et al. iScience 2021; 24: 102151.

“Exosomes provide unappreciated carrier effects that assist transfers of their miRNA to targeted cells; I. They are ‘The Elephant in the Room’”*

- Exosomes are a type of extracellular vesicle with diverse content that are released from stressed cells
- Micro-RNAs are short sequences of RNA that suppress selected proteins by binding to the promoter in their messenger RNA
  - There are thousands of different miRNAs each with specific functions
  - They survive well inside the protective coat of exosomes
  - Cell-cell communication is often carried out through the exchange of exosomes
- Exosomes released by immune cells are taken up by tissue cells to influence metabolic policy in the recipient cell through the specific miRNAs contained in the exosome

*Philip W. Askenase. RNA Biology 2021 May 4; 1-16.

Mitochondria, Lysosomes and Aging*

"Disruption of the mitochondrial–lysosomal axis coupled with abnormal EV [extracellular vesicle] secretion may play a role in the pathogenesis of aging and several disease conditions."

- Damaged mitochondria are normally cleared through an endosome-to-lysosome pathway
- When lysosomes are impaired, damaged mitochondria are excreted from the cell inside exosomes (extracellular vesicles)
- Excessive extracellular vesicles in the blood are a marker of aging

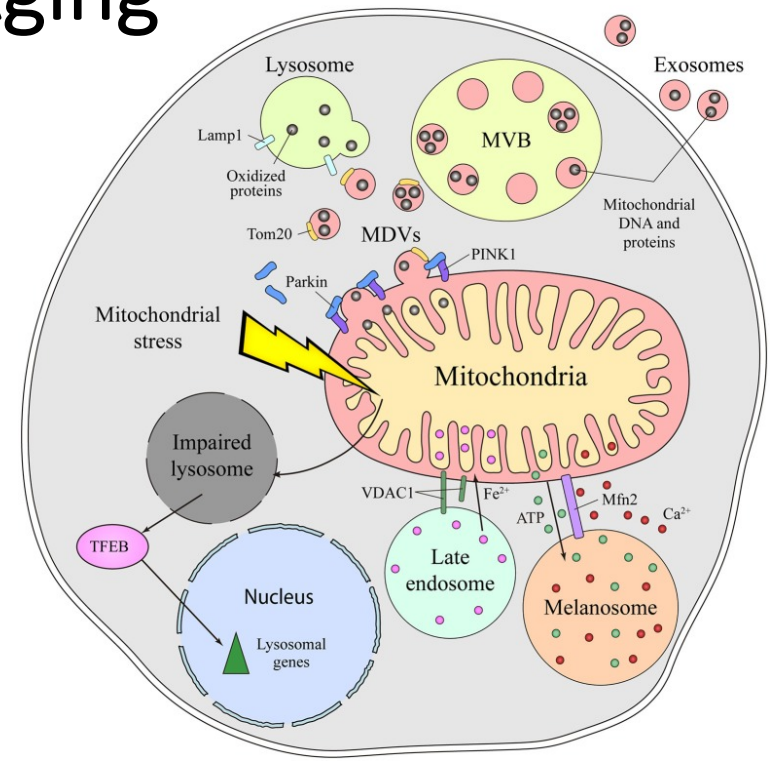
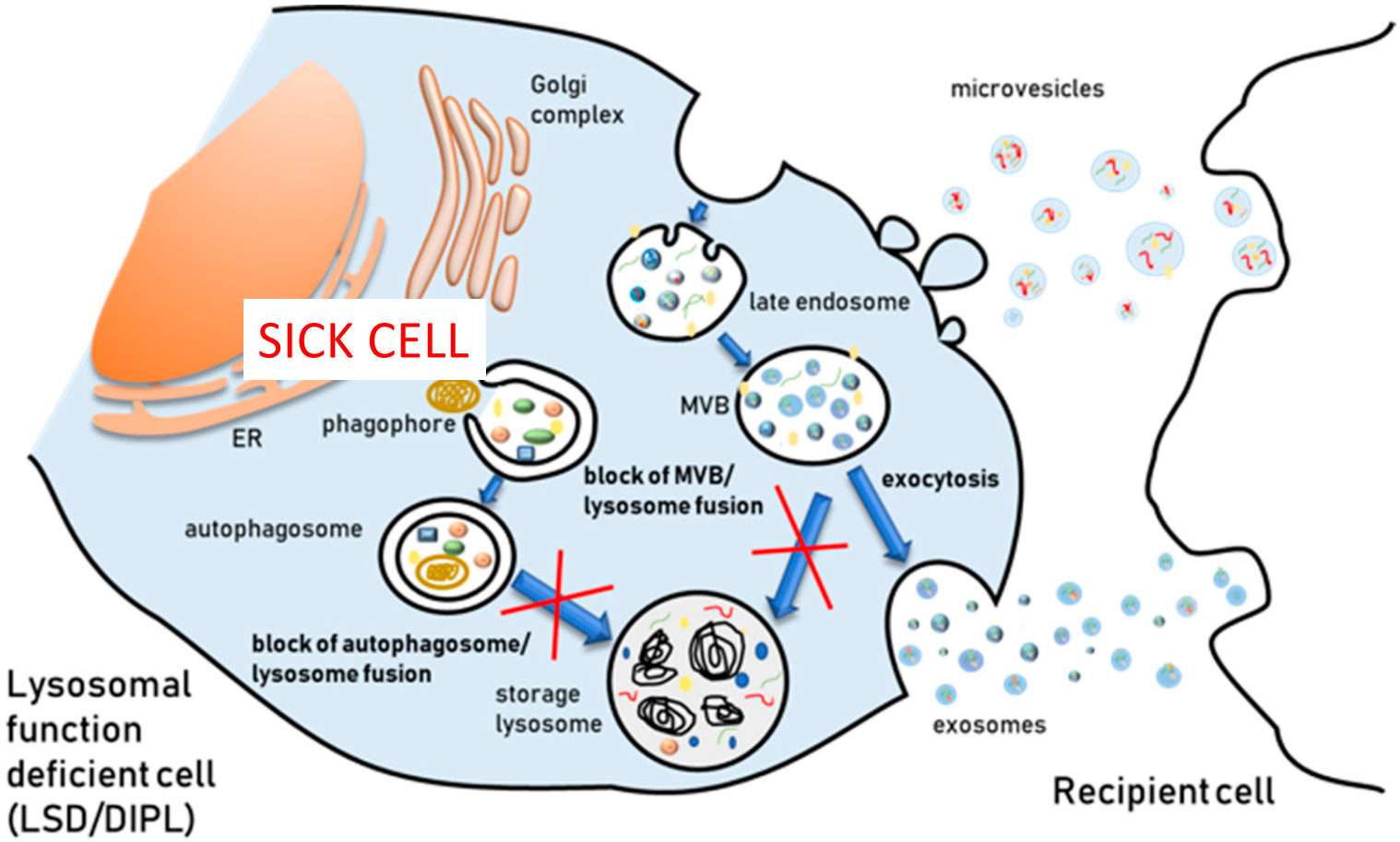


Figure 2 in GonzaloSoto-Heredero et al. Frontiers in Cell and Developmental Biology 2017; 5: 95.

*Anna Picca et al. Int J Mol Sci 2019; 20: 805.

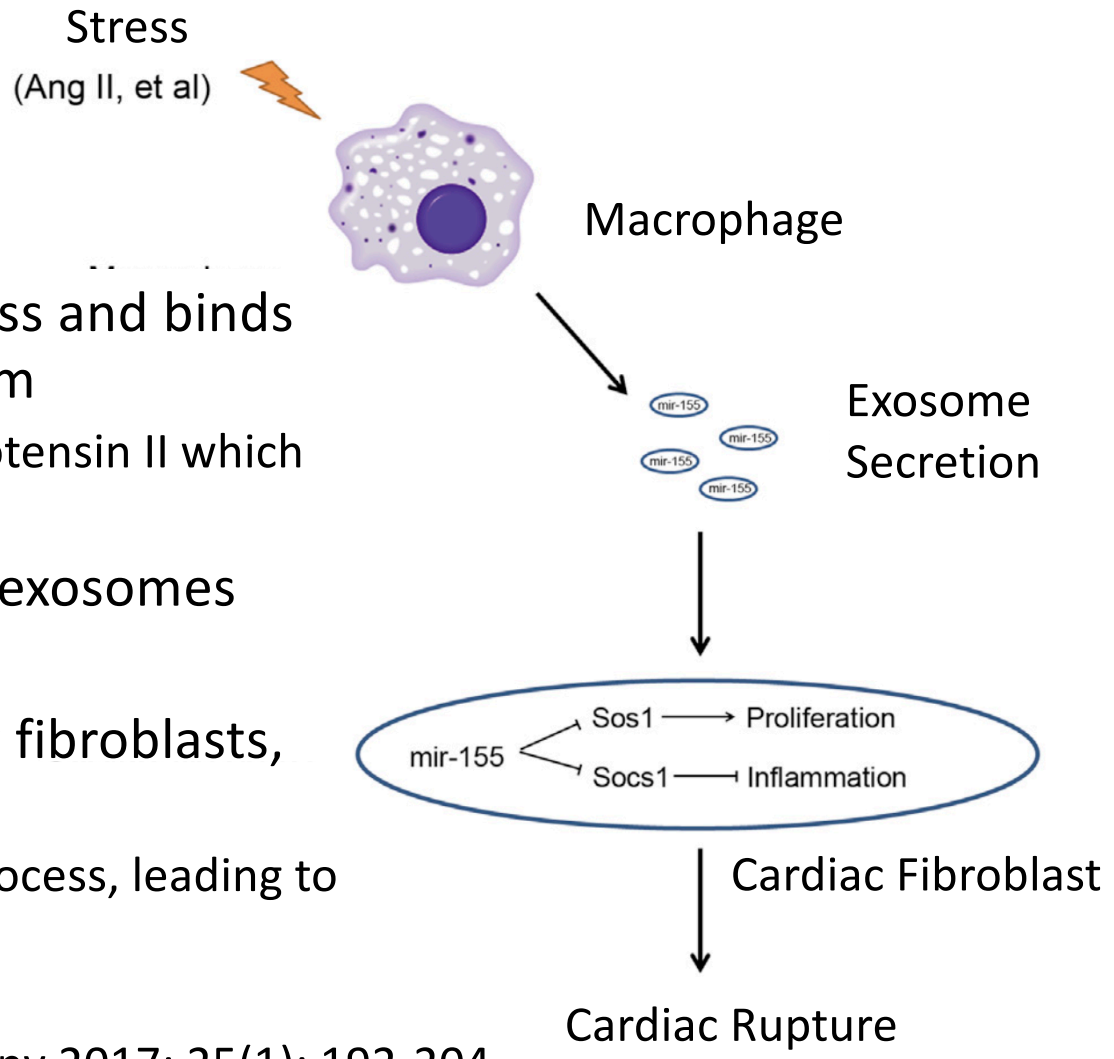
A cell that can’t clear its garbage dumps its garbage



*Brunella Tancini et al. Genes 2019; 10: 510.

How Spike Protein can Cause Cardiac Issues*

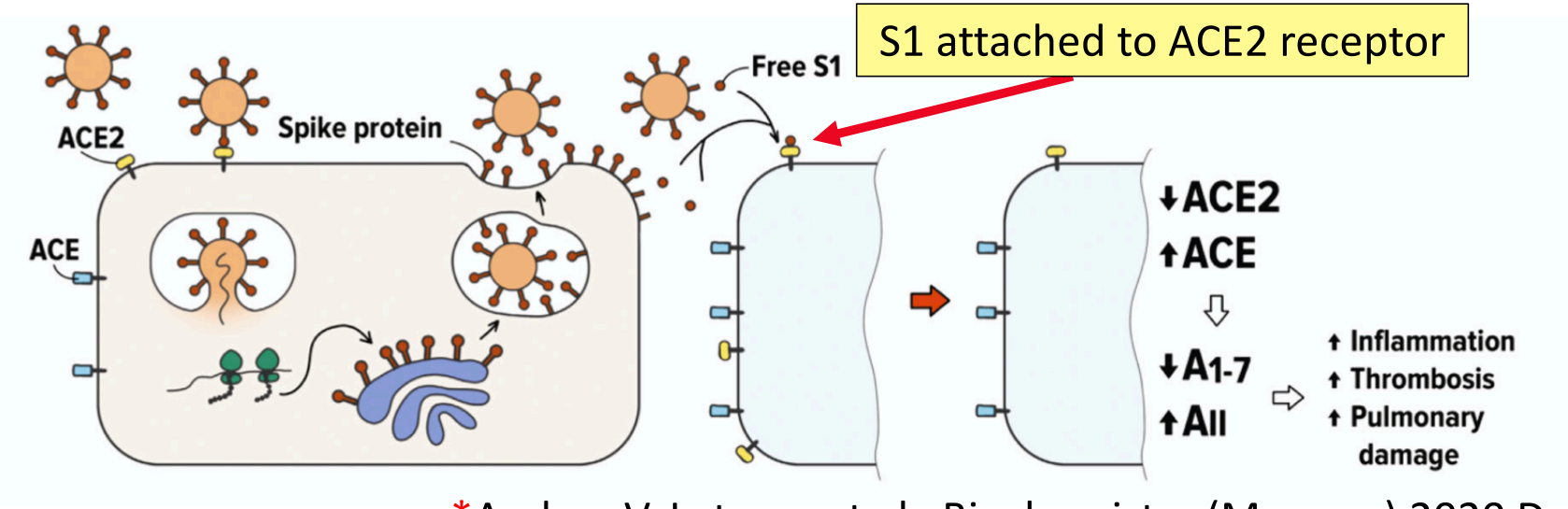
- Spike protein S1 unit causes stress and binds to ACE2 receptors, disabling them
  - This causes accumulation of Angiotensin II which activates macrophages
- Macrophages secrete abundant exosomes containing miR-155
- These exosomes are taken up by fibroblasts, suppressing their proliferation
  - This interferes with the healing process, leading to cardiac rupture



*Chunxiao Wang et al. Molecular Therapy 2017; 25(1): 192-204.

“Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection”*

Disabling ACE2 receptors causes Inflammation, thrombosis (blood clots) and damage to the lungs

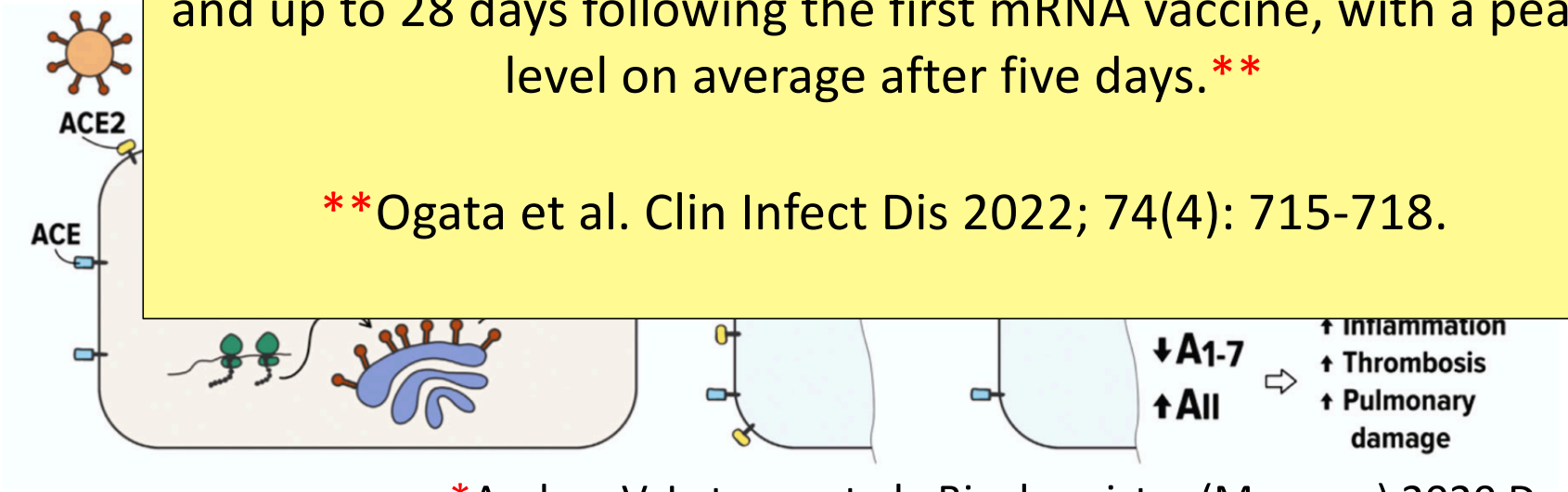


*Andrey V. Letarov et al. Biochemistry (Moscow) 2020 Dec 30: 1–5.

“Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection”*

Eleven out of 13 health care workers had detectable levels of spike protein and/or S1 in their blood plasma as early as 1 day and up to 28 days following the first mRNA vaccine, with a peak level on average after five days.**

**Ogata et al. Clin Infect Dis 2022; 74(4): 715-718.



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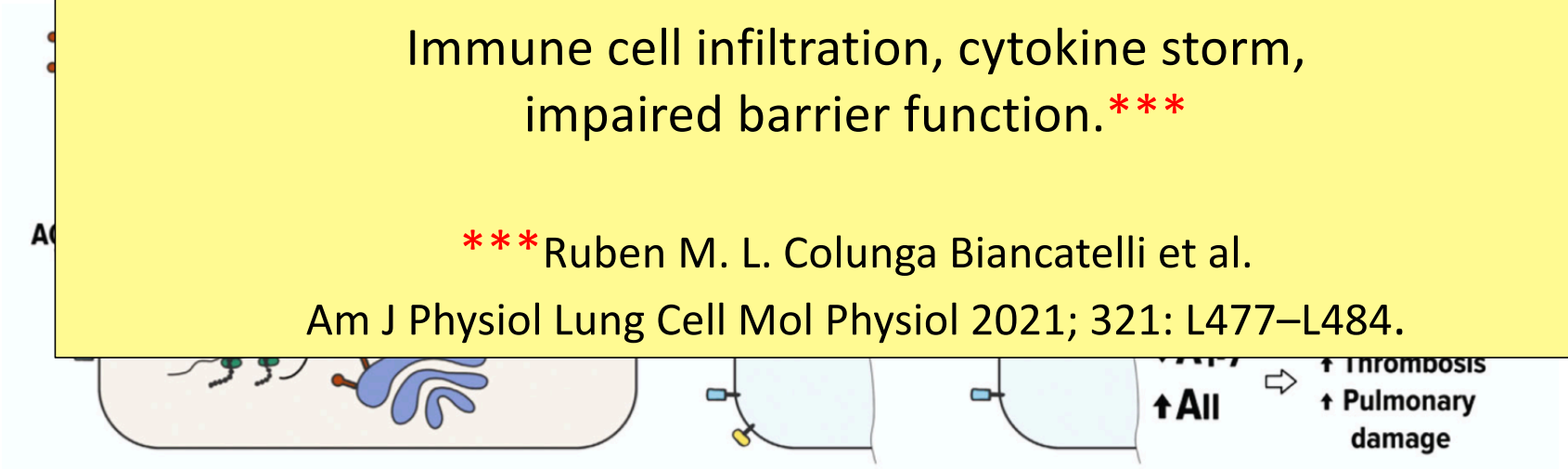
“Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection”*

S1 alone caused COVID-19-like lung symptoms in mice equipped with human ACE2 receptors:

Immune cell infiltration, cytokine storm, impaired barrier function.***

***Ruben M. L. Colunga Biancatelli et al.

Am J Physiol Lung Cell Mol Physiol 2021; 321: L477–L484.



*Andrey V. Letarov et al. Biochemistry (Moscow) 2020 Dec 30: 1–5.

DOI: 10.1111/acel.13128

ORIGINAL ARTICLE

Aging Cell WILEY

miR-155-5p inhibition rejuvenates aged mesenchymal stem cells and enhances cardioprotection following infarction *

- Expression of miR-155-5p was much higher in mesenchymal stem cells from aged donors compared to young donors
- miR-155-5p inhibited mitochondrial fission
- Upregulation of miR-155-5p in young MSCs led to increased cellular senescence
- Downregulation in aged MSCs decreased senescence markers

*Yimei Hong et al. Aging Cell. 2020;19:e13128.

miR-155 overexpression linked to worse outcomes in heart attack*

- Measured three miRNA levels in autopsy samples of 50 patients with MI

"innate immunity resulting in an intense inflammatory reaction plays an important role in the pathogenesis of the VR [ventricular rupture] after MI [myocardial infarction] in humans."

MI1: heart attack within first 24 hours of clinical symptoms
MI2: heart attack 2-7 days after onset of clinical symptoms

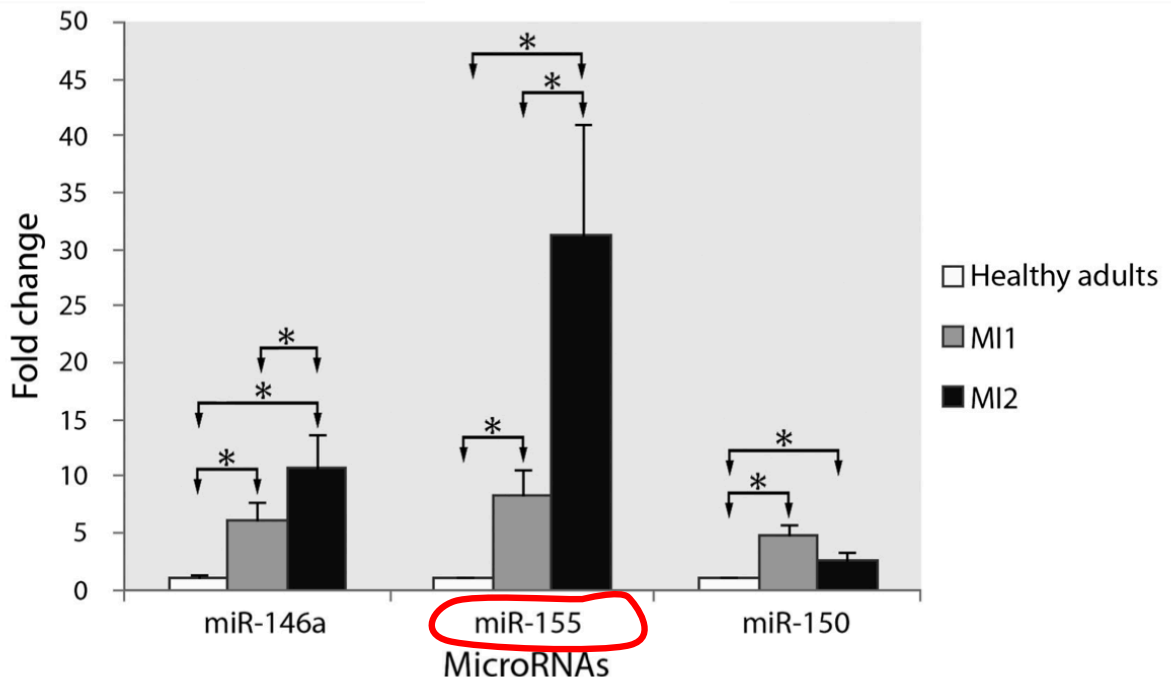
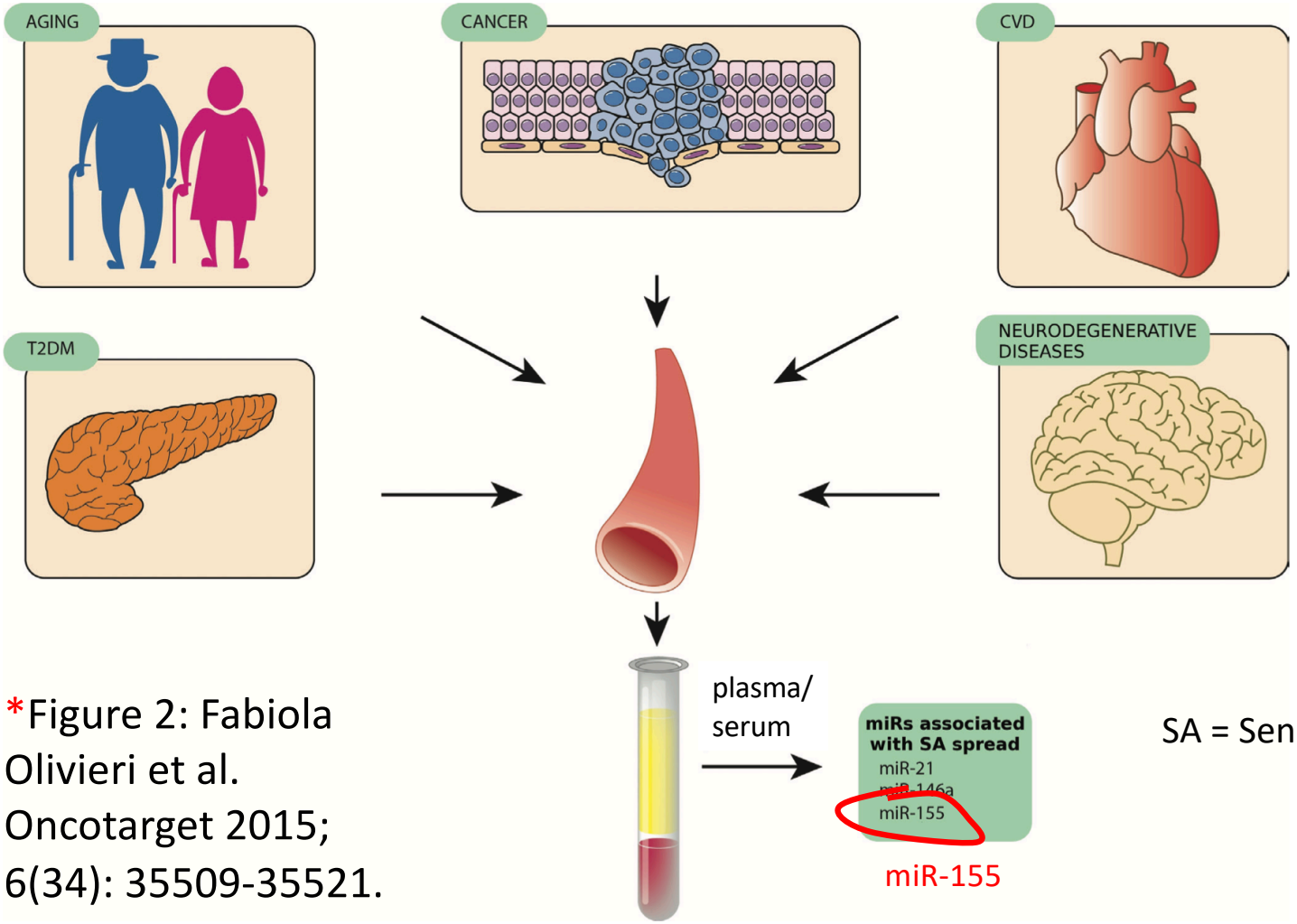


*Figure 1. Nina Zidar et al. Disease Markers 2011; 31: 259-265.

Number of events in VAERS for 2021 where cardiac symptoms were indicated*

Symptom	Covid-19 Vaccines	All Vaccines	Percent COVID-19
Myocarditis	2,322	2,361	98.3
Arrest	1,319	1,371	96.2
Arrhythmia	1,069	1,087	98.3
Heart attack	2,224	2,272	97.9
Heart failure	1,156	1,190	97.1
TOTAL	**8,090**	**8,281**	**97.7**

*S Seneff et al. Food and Chemical Toxicology 2022; 164: 113008.



DNA damage → senescence → inflammaging

*Figure 2: Fabiola Olivieri et al. Oncotarget 2015; 6(34): 35509-35521.

SA = Senescence Associated

Summary

- The mRNA vaccines are carefully crafted to induce immune cells to produce large quantities of the SARS-CoV-2 spike protein for a long time
  - The spike protein is neurotoxic and has prion-like characteristics
- The vaccines produce a strong antibody response in the spleen by activating germinal centers, and this increases susceptibility to prion disease
  - Exosomes traveling from the spleen to the brain may play a decisive role
- The spike protein by itself can disable ACE2, causing myocarditis
- There is much evidence from VAERS linking mRNA vaccines to neurodegenerative diseases and cardiovascular disease
- CJD can be induced within two weeks of mRNA vaccination, and 26 fatal cases have now been documented
- The vaccines likely promote a state of senescence via DNA damage and induction of specific microRNAs in both immune cells and tissue cells → *accelerated aging*